REMARKS

At the outset, the undersigned wishes to thank Examiner Tran for the courtesies extended during the March 5, 2007 interview.

Claims 1 and 17-19 have been amended to affirmatively recite, amongst other things, that the claimed compositions have from about 1 to about 10 weight % of a powdered wax, less than about 25 weight % of a disintegrant, and the transitional phrase comprising was amended to the transitional phrase consisting essentially of. Support for these amendments can be found throughout the specification at, for example, page 4, lines 9-11, page 4, line 23 to page 5, line 3, Examples 1-4, and original claim 10.

Claim 9 was cancelled without prejudice, the Applicants reserving to the right to re-introduce this claim in the present application or any application claiming the benefit of priority thereto. Claim 10 was amended to remove the reference to disintegrant, which was added to claim 1.

These amendments were made in view of the written description rejection described in more detail below and the claim interpretation set forth by the Examiner in making out the obviousness rejection.

It is submitted that no new matter has been added by the above amendments.

Claims 1, 3-8, 10-15, and 17-19 are currently pending in the present application.

Written Description Rejection

Claims 1, 3-15 and 17-19 were rejected under 35 USC §112, first paragraph, as failing to comply with the written description requirement. (Paper No. 20061209 at 2). Specifically, the Examiner contended that the rejected claims contain subject matter that was not described in the specification in such a way to convey that the inventors, at the time the application was filed, had possession of the claimed invention. In making the rejection, the Examiner contended that "[t]he claims doe not identify the structure, material or acts set forth in the specification that would be capable of carrying out the functional properties recited in the claims." (Paper No. 20061209 at 2).

Claim 9 has been cancelled. Therefore the rejection of claim 9 is believed to be moot.

Claims 1 and 17-19 have been amended to specifically require a specific amount of a powdered wax and a disintegrant in a specific amount. It is believed that these structural limitations overcome the instant written description rejection.

Enablement Rejection

Claims 1, 3-15, and 17-19 were rejected under 35 USC §112, first paragraph, as failing to comply with the enablement requirement. (Paper No. 20061209 at 2). The Examiner asserted that the claims contain subject matter that was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. (Paper No. 20061209 at 2-3). The Examiner stated that the claims lack the description of the possible genus with the recited functional characteristics and the claims recite an immediate release rate by 30 minutes in pH 5.8 buffer, however, the specification discloses a similar immediate release rate by 15 minutes in pH 5.8 buffer. (Paper No. 20061209 at 3). The Examiner concluded that it was "not clear from the specification when and how the tablet can exhibit similar release rates at two different times, 15 minutes and 30 minutes." (Paper No. 20061209 at 3).

Claim 9 has been cancelled. Therefore the rejection of claim 9 is believed to be moot.

Claims 1 and 17-19 have been amended to specifically require a specific amount of a powdered wax and a disintegrant in a specific amount. While it is not believed that undue experimentation would have been required to make and use the originally claimed invention, it is believed the above amendments overcome the instant rejection.

As to the dissolution testing carried out in Examples 1- 4, the data demonstrate that 100% of APAP (acetaminophen) was released according to the dissolution testing by 30 minutes in pH 5.8 buffer. The fact that some examples show 100% APAP released at 15 minutes does not remove the fact that 100% of the APAP is released by 30 minutes in pH 5.8 buffer. In other words, if 100% APAP is released at 15 minutes, then 100% APA is also released at 30 minutes. Because the data are consistent with the pending claims it is not seen where the data are not clear. Thus, in view of the amendments and remarks set forth above, withdrawal of the rejection is respectfully requested.

Obviousness Rejections

Claims 1, 3-15, and 17-19 were rejected under 35 USC §103(a) as being unpatentable over by Smith, US Patent No. 6,194,000 ("Smith"), or Harbit, US Patent No. 3,108,046 ("Harbit") in view of Joshi, U.S. Patent No. 5,030,447 ("Joshi") and U.S. Patent No. 4,894,234 ("Sharma") (Paper No. 20061209 at 3.)

For the reasons set forth below, the rejection, respectfully is traversed.

The disclosures of Smith, Harbit, and Joshi set forth is previous papers submitted during prosecution of the present application are incorporated herein by reference.

Sharma discloses

[57] **ABSTRACT**

A drug delivery system comprising a core material comprising a drug, and a hydrophobic matrix coating the core. The coating delays hydration of the drug and masks the taste of the drug. The coating comprises an emulsifier, an edible fatty acid or wax and a glyceride. The delivery system can be incorporated into various food products, pharmaceutical preparations and proprietary products.

The present invention concerns a drug delivery system capable of delaying hydration of the drug and masking the taste of the drug comprising:

(a) a drug; and

(b) a hydrophobic matrix comprising

(i) an emulsifier; and

(ii) an edible material having a melting point in the range of about 25° C. to about 100° C. selected from the group consisting of

(a) fatty acids having an iodine value of about 1 to about 10,

(b) natural waxes,

(c) synthetic waxes and

(d) mixtures thereof; and

(iii) at least one glyceride.

The inventive delivery systems and method of preparation solve the problems associated with surface wetting, uniform coating and delayed hydration encountered with conventional coatings and coating techniques.

Col. 2.

(iii) at least one glyceride.

The emulsifier is critical to the hydrophobic matrix and is believed to serve several important purposes. Most importantly, the emulsifier acts as a wetting agent to increase the affinity of the fat or wax to the core material surface. Fat and wax are often not compatible with various surfaces. The emulsifier mediates the poor affinity between these materials and allows for uniform wetting of the drug surface by the fat or wax. Uniform wetting of the surface is critical to proper adherence of the hydrophobic matrix coating and to the effectiveness of the ultimate protection it provides for the drug material.

Secondly, the emulsifier serves as a modifier of the rheological and thermal properties of the fat which lends it the capability of forming an elastic (non-brittle) and flexible film over a wider temperature range. Ordinary fat without the emulsifier would result in a brittle, porous crystalline coating which would be vulnerable to rupture during processing and which would fail to uniformly wet the core material drug (surface) Additionally, the emulsifier acts to modify the morphological properties of the fat or wax, as well as to increase their heat capacity, thereby retarding liquid to solid phase transitions and allowing for increased flexibility in processing conditions, e.g., the mixture can be processed in a specified temperature range for a longer period of time. The increased heat capacity plays an important role in the final delivery system since more heat will be required before the system melts down and releases the drug material. Thus, at short exposures to elevated temperatures, the delivery system will be more stable than without the addition of the emulsifier.

(Col. 3)

fatty acids.

The edible fatty acid or wax materials are employed in the instant delivery systems in amounts of about 61% to about 95% by weight of the delivery system, preferably in amounts of about 63% to about 90% and most preferably in amounts of about 66% to about 80%. These amounts are necessary to adequately coat the surface of sweeteners such as aspartame which have a high surface area to weight ratio. Hydrogenated palm oil is the most preferred fatty acid. Paraffin wax and mirocrystalline wax are the preferred waxes.

The edible fatty acid or wax component is critical to the effectiveness of the protective barrier. The hydrophobic matrix, of which the fatty acid or wax is an essential part, provides protection for the core material from heat, light, moisture, pH, reactive chemicals and the like. Additionally, the release of the drug material is controlled via the hydrophobic matrix and can serve other purposes such as the masking of taste for unpalatable or unpleasant tasting materials.

The term glyceride component used herein refers to

(Col. 4)

(j) Antipyretics and analgesics such as acetaminophen aspirin and ibuprofen;

(Col. 5)

In making the rejection as to Smith, the Examiner asserted that

Smith teaches an analgesic composition comprising immediate and controlled release forms (see abstract). The immediate release comprises up to 90% of the analgesic agent, polyethylene glycol, waxes, and other carriers (column 2, lines 39-50; and column 3, lines 29-51). The dosage form provides from about 1-5000 mg/day of the analgesic agent (ID). The composition is in for oral administration in tablet or

(Paper No. 20061209 at 3.)

capsule or granule form (column 2, lines 55-67). Suitable coating to provide sustained release comprises cellulose derivatives polymer (column 4, lines 26-45).

(Paper No. 20061209 at 4.)

As to Harbit, the Examiner asserted that

Harbit teaches a high dose tablet comprising from about 75% to about 98% drug and wax, such as paraffin wax or shellac wax (column 3, lines 1-31). The tablet dosage further comprises lubricant (column 4, lines 9-19). The dosage form provides both immediate release and sustained release (column 4, lines 21-31).

(Paper No. 20061209 at 4.)

The Examiner acknowledged, however, that the cited documents do not explicitly teach acetaminophen.. (*Id.* at 4.)

To fill the acknowledged gap, the Examiner relied upon Sharma for "teach[ing] analgesic include[ing] acetominophen." (*Id.*) The Examiner concluded:

> includes acetaminophen (column 5, lines 54-55). Thus, it would have been obvious to prepare an acetaminophen composition in view of the teaching of Sharma, because Sharma teaches analgesic includes acetaminophen, aspirin, or ibuprofen, and because Smith and Harbit teach compositions suitable for analgesic active agents.

(*Id.*)

The Examiner also stated:

> Smith or Harbit does not explicitly teach wax in powder form. Joshi teaches a tablet dosage form comprising wax in finely powdered form having size less than 500 µm such as microcrystalline wax, carnauba wax, or paraffin (column 2, lines 22-24). Thus, it would have been obvious to one of ordinary skill in the art to modify the wax in the tablet dosage of Smith or Harbit using the finely powdered wax in view of the teaching of Joshi, because Joshi teaches a composition include one or more powder wax result in an excellent storage stable even thought it includes a medicament which may degrade in a low pH environment (column 1, lines 37-40), because Smith or Harbit teaches the use of wax in tablet dosage form comprising active agents.

Claim 9 has been cancelled. Therefore the rejection of claim 9 is believed to be moot.

Binding precedent is clear that the "[d]etermination of obviousness cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention." ATD Corp. v. Lydall, Inc., 159 F.3d 534, 546, 48 USPQ2d 1321, 1329 (Fed. Cir. 1998). There must be a teaching or suggestion within the prior art, within the nature of the problem to be solved, or within the general knowledge of a person of ordinary skill in the field of the invention, to look to particular sources, to select particular elements, and to combine them as combined by the inventor. See Ruiz v. A.B. Chance Co., 234 F.3d 654, 665, 57 USPQ2d 1161, 1167 (Fed. Cir. 2000); ATD Corp, 159 F.3d at 546, 48 USPQ2d at 1329; Heidelberger Druckmaschinen AG v. Hantscho Commercial Prods., Inc., 21 F.3d 1068, 1072, 30 USPQ2d 1377, 1379 (Fed. Cir. 1994) ("When the patented invention is made by combining known components to achieve a new system, the prior art must provide a suggestion or motivation to make such a combination.").

As admitted by the Examiner: Smith discloses a composition having an immediate release form and a sustained release form and Harbit discloses a sustained release tablet. It is not seen where either of these cited documents disclose or suggest tablets that are immediate release tablets consisting essentially of, among other things, acetaminophen, powdered wax and a disintegrant. The dosage forms disclosed are either

sustained release or a combination of immediate release and sustained release. It is not seen where Joshi or Sharma would close this gap. Thus it is not seen where one of ordinary skill in the art of immediate release tablets would look to Smith or Harbit to solve the problem of making an immediate release tablet as claimed. For this reason, the rejection is improper and should be withdrawn.

In addition, it is not seen where there is any suggestion or motivation to use the specific amount of powdered wax and disintegrant as in the currently amended claims. For this additional reason, the rejection is improper and should be withdrawn.

Further, as to the current amendments, it is not seen where any of the documents disclose or suggest acetaminophen as an ingredient or the fact that the acetaminophen is released from the swallowable immediate release tablet by 30 minutes in pH 5.8 buffer. For this additional reason, the rejection is improper and should be removed.

Claims 1-15 and 17-20 were rejected under 35 USC §103(a) as being unpatentable over by Smith or Harbit, in view of Sharma, WO 01/21155, ("Remon") and Mueller, U.S. Patent No. 5,643,984 ("Mueller") (Paper No. 20061209 at 5.)

For the reasons set forth below, the rejection, respectfully is traversed.

The disclosures of Smith, Harbit, Remon, and Mueller set forth in previous papers submitted during prosecution of the present application are incorporated herein by reference. Sharma's disclosure set forth above in incorporated herein by reference.

(p. 24 ln. 16 – p. 25, ln.1.)

In making the rejection, the Examiner stated:

> Smith or Harbit in view of Sharma are relied upon for the reason stated above. The references do not explicitly teach wax in powder form. Remon discloses a rapidly disintegrating tablet comprising an active agent and wax (page 10, lines 14-18; page 19, lines 10-21). Wax includes microcrystalline wax or a natural wax (page 11, line 7 through page 15, line 8). The composition further contains disintegrants, swellable materials as well as other fillers (page 15, line 9 - page 18, line 6). Active agents are chosen from a wide variety of known pharmaceutical agents (page 19, line 22 - page 20, line 18). The composition also includes a film coating (page 21, line 4 - page 22, line 8). The tablets are produced by compression (page 23, lines 3-9). The tablets are rapid disintegration tablets (page 24, line 16 - page 25, line 1).
>
> Remon does not expressly teach the particle size of the microcrystalline wax. Mueller teaches typical microcrystalline hydrocarbon waxes having particle size within the range of about 1 μm to about 300 μm (column 2, lines 55-65). Thus, it would have been obvious for one of ordinary skill in the art to use microcrystalline wax in view of the teachings of Remon and Mueller for the composition taught by Smith or Harbit, because Remon teaches the use of wax in tablet dosage form that disintegrate rapidly in water (page 9, lines 5-10), because Smith or Harbit teaches the use of wax in tablet dosage form, and because Mueller teaches microcrystalline wax having particle size within the claimed range is known and typical.

(Paper No. 20061209 at 5.)

The Examiner asserted that the "present claims do not preclude sustained release." It is submitted the current amendment in the transition phrase to consisting essentially of overcomes this matter. Therefore, it is submitted that claims are in allowable condition and the rejection should be withdrawn.

The Examiner asserted that while the cited references do not teach the release rate by 30 minutes in pH 5.8 buffer, the stated that burden was on the Applicants to show that the cited documents do not have this release properties. With all do respect, in view of the amendments to the claims and the arguments set forth in this paper, it is not believed that a prima facie cases of obviousness has been made by the Examiner. Therefore, the burden has not shifted to the Applicants. For this reason, the rejection is improper and should be withdrawn.

It is well established that a reference will teach away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant. *In re Gurley,* 27 F.3d 551, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994).

As admitted by the Examiner, Smith discloses a composition having an immediate release form and a sustained release form, and Harbit discloses a sustained release tablet. None of Smith, or Harbit discloses a dosage form that provides immediate release. The Examiner then relied on Remon for disclosing, among other things, a rapidly disintegrating tablet. However, it is not seen where Remon disclose or even suggests the desirability of a **swallowable immediate release tablet**. In fact, it is respectfully submitted that Remon teaches away from a **swallowable** tablet, including an immediate release swallowable tablet.

Remon specifically recites "the solid shaped articles of the present invention ….provide[s] a formulation which distintegrates rapidly in water to form an instantaneous suspension of adequate viscosity to be swallowed without premature releast from controlled release particles….or an immediate release suspension…[which] is useful … for young children and elderly patients **who cannot swallow tablets or capsule**s, or for patients who require large doses of biologically active ingredients, where swallowing large dosage forms is difficult." Remon at 24-25. Thus, it is not seen where any tablet produced by Remon would be a swallowable immediate release tablet per se, much less a swallowable immediate release tablet useful in obtaining the result sought by the present invention. Thus, to the extent the rejection relies on Remon, it is submitted that Remon teaches away from the present invention and the rejection is improper and should be withdrawn.

Binding precedent is clear that the "[d]etermination of obviousness cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention." *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 546, 48 USPQ2d 1321, 1329 (Fed. Cir. 1998). There must be a teaching or suggestion within the prior art, within the nature of the problem to be solved, or within the general knowledge of a person of ordinary skill in the field of the invention, to look to particular sources, to select particular elements, and to combine them as combined by the inventor. *See Ruiz v. A.B. Chance Co.*, 234 F.3d 654, 665, 57 USPQ2d 1161, 1167 (Fed. Cir. 2000); *ATD Corp,* 159 F.3d at 546, 48 USPQ2d at 1329; *Heidelberger Druckmaschinen AG v. Hantscho Commercial Prods., Inc.*, 21 F.3d 1068, 1072, 30 USPQ2d 1377, 1379 (Fed. Cir. 1994) ("When the patented invention is made by combining known components to achieve a new system, the prior art must provide a suggestion or motivation to make such a combination.").

It appears that the Examiner has culled facts from disparate documents in an attempt to make a *prima facie* case of obviousness. However, a *prima facie* case of obviousness cannot ignore the fundamental aspect of the invention, viz., a swollowable immediate release tablet. It is submitted that none of the documents relied on the by Examiner appear to be directed to swallowable immediate release tablets. For this reason, the rejection is improper and should be withdrawn.

Finally, the Examiner is invited to call the applicants' undersigned representative if any further action will expedite the prosecution of the application or if the Examiner has any suggestions or questions concerning the application or the present Response. In fact, if the claims of the application are not believed to be in full condition for allowance, for any reason, the applicants respectfully request the constructive assistance and suggestions of the Examiner in drafting one or more acceptable claims pursuant to MPEP §707.07(j) or in making constructive suggestions pursuant to MPEP §706.03 so that the application can be placed in allowable condition as soon as possible and without the need for further proceedings.

Respectfully submitted,

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